NMT MEDICAL

The CardioSEAL® Septal Occlusion System
Instructions for Use for PFO closure
Table of Contents

INSTRUCTIONS FOR USE

The CardioSEAL Septal Occlusion System
Federal law (USA) restricts this device to sale by or on the order of a physician (or properly licensed practicioner).

1. HUMANITARIAN USE DEVICE: Authorized by Federal law for use in the treatment of patients with a patent foramen ovale (PFO) with recurrent cryptogenic stroke due to presumed paradoxical embolism through a patent foramen ovale and who have failed conventional drug therapy.

The effectiveness of this device for use in this indication has not been demonstrated.

2. PRODUCT DESCRIPTION:
The CardioSEAL Septal Occlusion System consists of two primary components:

- The CardioSEAL (Occluder), which is constructed of a metal (MP35n) framework to which polyester fabric is attached, and
- The Delivery Catheter, a coaxial polyurethane catheter designed specifically to facilitate attachment, loading, delivery and deployment of the CardioSEAL to the defect.

3. INDICATION FOR USE:
The CardioSEAL Septal Occlusion System is authorized by Federal (USA) law as a Humanitarian Use Device for use in the following indication only:

> The CardioSEAL Septal Occlusion System is indicated for the closure of a patent foramen ovale (PFO) in patients with recurrent cryptogenic stroke due to presumed paradoxical embolism through a patent foramen ovale and who have failed conventional drug therapy.
>
> Cryptogenic stroke is defined as a stroke occurring in the absence of potential phanerogenic cardiac, pulmonary, vascular or neurological sources. Conventional drug therapy is defined as a therapeutic INR on oral anticoagulants.

The effectiveness of this device in this indication has not been demonstrated.

4. CONTRAINDICATIONS:
Presence of thrombus at the intended site of implant, or documented evidence of venous thrombus in the vessels through which access to the defect is gained.

Active endocarditis, or other infections producing a bacteremia.

Patients whose vasculature, through which access to the defect is gained, is inadequate to accommodate the appropriate size sheath.

Patients whose defect is too small to allow the 11 F sheath to cross the defect.

Anatomy in which the CardioSEAL size required would interfere with other intracardiac or intravascular structures, such as valves or pulmonary veins.

Patients with coagulation disorders who are unable to take antiplatelet or, anticoagulant therapy.

Patients with known hypercoagulable states.

Patients with an intra-cardiac mass or vegetation.

5. WARNINGS:

This device should only be used by those physicians trained in transcatheter defect closure techniques, and by those physicians prepared to provide long term follow up patient monitoring.

Physicians attempting to recover an embolized device should be limited to those that have completed appropriate device retrieval technique training.

> Embolized CardioSEAL devices should be removed. Dislodged CardioSEALs have embolized to the pulmonary and systemic vasculature.
>
> Embolized CardioSEALs may disrupt critical cardiac functions. Physicians must be prepared to deal with urgent requirements to extract or move embolized CardioSEALs that result in critical hemodynamic compromise.
>
> Embolized CardioSEALs should not be withdrawn through intracardiac structures unless they have been adequately collapsed within a sheath. Devices that are not adequately collapsed within a sheath may entangle with valvular or other cardiac structures.

Do not attempt to repair or reuse damaged product. Do not reuse or resterilize product. Return to manufacturer.

Surgical support should be readily available if needed.

Transient hemodynamic compromise may be encountered during device placement, which may require fluid replacement or other medications as determined by the physician.

6. PRECAUTIONS:

6.1 CardioSEAL – Handling Precautions

Do not use the system if, during loading of the CardioSEAL, difficulty is encountered in transferring the CardioSEAL into the loader or from loader to the pod of the delivery catheter.

Do not modify the delivery catheter or CardioSEAL. Modification may result in damage that can result in complications such as embolism, framework fracture, failure to release, and improper seating at the target defect.

6.2 CardioSEAL – Sizing Precautions

The use of a compliant balloon catheter to determine defect localization is recommended.

Accurate defect sizing is critical to CardioSEAL selection. Defect sizing methods, such as contrast angiography, echocardiography and – or balloon sizing should be considered as procedural alternatives.

The anatomic area surrounding the target defect should have enough contiguous structure to support the CardioSEAL.

The defect and surrounding structures should be fully examined in multiple planes to assure proper sizing of the CardioSEAL and to detect any unusual anatomy.

6.3 CardioSEAL – Procedural Precautions

The ability of the patient to remain still during implantation must be weighed against the need for "conscious" sedation versus general anesthesia. The decision to use general anesthesia in any individual patient is subject to physician judgement.

Patients should be fully heparinized throughout the procedure using adequate dosing so as to keep the ACT greater than 200 msec.

Antibiotic therapy periprocedurally is recommended to reduce the risk of perioperative infection.

The use of Transesophageal Echocardiography (TEE) should be considered as a potential aid in placing the CardioSEAL. If used, the patient's esophageal anatomy must be adequate for placement and manipulation of the TEE probe.

Placement of the CardioSEAL requires the use of fluoroscopic X-ray guidance. The risk of increased x-ray exposure for patients who are pregnant must be weighed against the potential benefits of the technique.

The patient's vasculature should be sufficient to accommodate the 11 F sheath required to deliver the CardioSEAL.

Introducer sheaths longer than 80 cm will prohibit the complete extrusion of the CardioSEAL from the sheath during delivery to the defect.

A delivery catheter of equivalent or larger pod size must be used with the CardioSEAL to avoid damage to the implant during loading and deployment.

Care should be taken not to entrap right atrial Chiari networks or large Eustachian valves under the right atrial side of the device.

Malpositioned CardioSEALs may interfere with cardiac, vascular or valvular structures, depending on patient anatomy. Physicians should consider removing malpositioned CardioSEALs in these patients.

6.4 CardioSEAL – Post Implant Precautions

The time course of endothelialization of the device is unknown. Patients should receive appropriate endocarditis prophylaxis for the six months following implantation. The decision to continue prophylactic treatment after six months is subject to physician judgement.

Patients should be treated with antiplatelet/anticoagulation therapy, (see Section 8 Clinical Studies for the dosage used in the High-risk study) for six-months following implant. The decision to continue medical treatment beyond six months is subject to physician judgement.

If a left sided thrombus is identified, the patient should be evaluated for a hypercoagulable state and initiation of aggressive anticoagulant therapy should be given. Thrombolysis and surgical removal should be considered if the patient does not respond to the anticoagulant therapy.

All CardioSEALs are non-ferromagnetic. Independent studies of CardioSEAL in a 1.5 Tesla magnetic field demonstrate no movement of the CardioSEAL. However, MRI image quality may be compromised in the area of the implant.

7. ADVERSE EVENTS:

7.1 Observed Adverse Events:

In a 292 patient multi-center High Risk study, 35 patients underwent closure of a PFO to prevent neurological injury. Six (6) patients had failed conventional drug therapy as evidenced by a recurrent stroke and 29 were at risk of a neurologic injury for the following reasons: recurrent embolic events despite medical therapy (9); a medical or occupational contraindication to anticoagulation (17); could not tolerate anticoagulation (2); and presence of a thrombus in the right atrium (1).

One patient died of lung cancer while in the study. Eighteen (18) patients have completed a 12 month follow-up visit and five patients completed a 24 month visit.

A total of 44 adverse events were recorded among the 35 patients enrolled in the study for closure of their PFO. These adverse events were classified as Serious (4), Moderately Serious (16), Not Serious (23), or Unknown Seriousness (1) and were linked to either the device, the implant procedure, the catheterization procedure, or other causes, such as a pre-existing condition. Of these 44 adverse events, 7 events were definitely, probably or possibly related to the device, the implant procedure, or the catheterization. All 7 of these events were classified as moderately serious (Table 1).

Adverse Events – Table 1 PFO (n=35)		
	Moderately Serious	
	Early Event*	Late Event**
Device Related		
Transient Neurological symptoms	2	0
Implant Procedure Related		
None	0	0
Catheterization Procedure Related		
ST elevation	1	0
Brachial plexus injury	1	0
Rash	1	0
Pseudoaneurysm at vascular access site	1	0
Tachycardia	1	0

* = Early event is ≤ 30 days from implant. Total =1 early event.
** = Late event is > 30 days from implant. Total =0 late events.

In this study, fractures of the framework have been reported in 9 out of 35 implanted patients. The risk of fracture appears to be related to the size of the Occluder selected relative to the size of the heart chamber. There have been two reports of palpitations which were considered possibly related to device arm fracture. In both cases, they were classified as not serious.

7.2 Potential Adverse Events:

Placement of the CardioSEAL involves using standard interventional cardiac catheterization techniques. Complications commonly associated with these procedures include, but are not limited to:
Air Embolus
Allergic dye reaction
Anesthesia reactions

Apnea
Arrhythmia
Death
Fever
Headache / Migraines
Hematoma and/or Pseudoaneurysm including blood loss requiring transfusion
Hypertension; Hypotension
Infection including Endocarditis
Perforation of Vessel or Myocardium
Stroke / Transient Ischemic Attack
Thromboemobolic events
Valvular regurgitation.

7.3 Observed Device Malfunctions:

There were no reports of device malfunctions in this PFO population. However, there were 4 device malfunctions in a supporting cohort of patients with atrial level defects. These malfunctions included: one report of a kink in the delivery system, identified during the device placement; one report of a difficult release, the device was subsequently not used; one report of a device which did not open the device was subsequently not used; and one report of difficulty advancing the device through the pod resulting from the physician modifying the delivery system. There were no clinical sequelae associated with any of these device malfunctions.

8. CLINICALSTUDIES:

Study Design/Objective: The multi-center clinical trial conducted by Children's Hospital, Boston, Massachusetts, is a prospective, non-randomized trial studying the use of the CardioSEAL® Septal Occlusion system to close a variety of hemodynamically significant cardiac defects (e.g., fenestrated fontans, ventricular septal defects, atrial septal defects). The risks of surgical closure for the patients enrolled in this trial are sufficient to justify the known and potentially unknown risks of transcatheter closure with the CardioSEAL device. The study (referred to as the High-risk study) is ongoing and is summarized below. Data from patients undergoing PFO closure, who had failed conventional drug therapy as evidenced by a recurrent stroke, was extracted from this study as well as patients who were at risk of a neurologic injury for the following reasons: recurrent embolic events despite medical therapy ; a medical or

occupational contraindication to anticoagulation; could not tolerate anticoagulation ; and presence of a thrombus in the right atrium.

Patient Entry: Patients were eligible for enrollment in the High risk study if they had a defect(s) of sufficient size to require closure, but were considered to be at high risk for surgical closure, due to either complex medical or cardiac disease. An independent peer review group determined whether a patient should be enrolled into the trial based on the following criteria:

- the patient had a type of defect that was technically difficult or impossible to close surgically, such that the surgical risks were sufficient to justify the known and potential unknown risks of the device, or
- the patient's overall medical condition was such that the surgical risks were sufficient to justify the known and potential unknown risks of the device.

Methods: After enrollment, patients underwent cardiac catheterization. Position and size of the defect were confirmed by angiography. A hemodynamic assessment was performed pre-implant, and after test occlusion of the defect with a balloon. When these data suggested that the defect contributed to unfavorable hemodynamics and was feasible for transcatheter closure, device placement proceeded. Patients received aspirin, 1mg/kg/day, rounded to the nearest half tablet of 80 mg size, for at least six months following the procedure.

Patients were seen for follow up assessments as described in Table 2:

Timing of Evaluations – Table 2

	Pre-Implant	Pre-D/C	1 month F/U	6 month F/U	12 month F/U	24 month F/U
Cardiac HX/PE	X	X	X	X	X	X
Chest X-Ray	X	X	X	X	X	
Fluoroscopy				X		X
Echo/Doppler	X	X	X	X	X	X
EKG (rhythm)	X	X	X	X	X	X
Clinical Status	X	X	X	X	X	X

Primary Endpoints: A 6-category ordinal scale was used to measure clinical status. The scale takes values from 0 to 5, and was constructed so that an improvement by one category would be clinically relevant.

The Clinical status scale consists of seven different classes representing important aspects of overall cardiac and medical status: right to left shunt, left to right shunt, risk for systemic emboli, hemodynamic compromise not due to shunt, arrhythmia, elevated pulmonary vascular resistance, and medical illness. The condition most closely related to a patient's indication for device closure is identified, and the patient is placed in the lowest possible category according to criteria for that class.

All of the patients undergoing device placement for PFO closure to prevent neurological injury are evaluated using the criteria in Table 3 for patients with systemic emboli. A trivial or no residual leak status was considered the same as having no intracardiac potential for emboli. Embolic events, presumed or confirmed to be due to emboli include, both transient or permanent events resulting in symptoms.

Table 3 Clinical Status Scale

Category	0	1	2	3	4	5
Systemic embolic	N/A	recurrent embolic events, on Coumadin	Recurrent embolic events, but no anticoagulant	single embolic event	potential for embolic event	no intra-cardiac potential for emboli

Note: a deceased patient is rated as -1 on the Clinical Status Scale.

Additionally an assessment of the echocardiographic closure status was made at each time point both at the evaluating facility, and by an unaffiliated core laboratory. Residual flow was assessed using Doppler color flow mapping, and graded using the following guidelines:

"Trivial" to "Absent": barely detectable or no detectable residual color flow through the defect. If flow is present, it is a single color flow jet, well-circumscribed, with a proximal jet width measuring less than 1 mm in diameter in all views.

"Small": single color flow jet, well-circumscribed, and measuring 1-2mm (maximal proximal width) in all views in infants and children weighing less than 20 kg, or between 1 and 3 mm in diameter in larger children and adults.

"More than small": single color flow jet, well-circumscribed, measuring greater than 2 mm in diameter in all views in infants and children weighing less than 20 kg, or greater than 3 mm in diameter in all views in larger children and adults.

Results: At the time the PFO data was analyzed, 6 patients who had failed conventional drug therapy as evidenced by a recurrent stroke and 29 patients who were at risk of a neurologic injury for the following reasons: recurrent embolic events despite medical therapy (9); a medical or occupational contraindication to anticoagulation (17); could not tolerate anticoagulation (2); and presence of a thrombus in the right atrium (1) were enrolled in the study for PFO closure. Enrollment occurred at four investigational sites.

Among the 6 patients treated with a CardioSEAL device who had failed conventional drug therapy as evidenced by a recurrent stroke, there were 3(50%) males and 3 (50%) females. The age of the patients ranged from 35.4 years to 60.7 years, with a median age of 48.8 years.

Among the 29 patients treated with a CardioSEAL device who were at risk of a neurologic injury, there were 14(48.3%) males and 15 (51.7%) females. The age of the patients ranged from 5.3 years to 73.2 years, with a median age of 34.7 years.

Device placement was successful in all 35 patients in whom an implant was attempted. A single device was implanted in each patient. Device sizes included: (6) 23mm, (9) 28mm, (18) 33mm and (2) 40mm device. All of the implanted devices remained stable throughout the follow-up period. None of the devices embolized or were explanted.

Table 4A reflects the number of patients observed within each clinical status category at each visit for the 6 patients who had failed conventional drug therapy as evidenced by a recurrent stroke.

Clinical Status by Lesion - Table 4A

	Category									
Timepoint	-1	0	1	2	3	4	5	Uncertain	Missing	Not Due
Initial	0	0	6	0	0	0	0	0	0	0
Discharge	0	0	0	0	0	2	3	1	0	0
1 Month	0	0	0	0	0	1	4	0	1	0
6 Month	0	0	0	0	0	0	2	1	3	0
12 Month	0	0	0	0	0	1	4	1	0	0
24 Month	0	0	0	0	0	0	0	0	1	5

Table 4B reflects the number of patients observed within each clinical status category at each visit for the 29 patients who were at risk of a neurologic injury.

Clinical Status by Lesion Table 4B

	Category									
Timepoint	-1	0	1	2	3	4	5	Uncertain	Missing	Not Due
Initial	0	0	9	3	16	1	0	0	0	0
Discharge	0	0	1	0	1	8	16	3	0	0
1 Month	0	0	0	1	0	5	17	3	3	0
6 Month	0	0	0	0	0	4	16	3	0	6
12 Month	1	0	0	0	0	1	7	4	1	15
24 Month	0	0	0	0	0	0	5	0	2	22

Table 5A reflects the number of patients observed within each Echo Closure category at each visit for the 6 patients who had failed conventional drug therapy as evidenced by a recurrent stroke.

Echo Closure Status - Table 5A

	Category					
	None-Trivial	Small	Greater than small	Uncertain	Missing	Not due
Initial	0	2	0	4	0	0
Discharge	1	1	0	4	0	0
1 Month	1	1	0	2	2	0
6 Month	3	0	0	1	2	0
12 Month	4	1	0	0	1	0
24 Month	0	0	0	0	1	5

Table 5B reflects the number of patients observed within each Echo Closure category at each visit for the 29 patients who were at risk of a neurologic injury.

Echo Closure Status - Table 5B

	Category					
	None-Trivial	Small	Greater than small	Uncertain	Missing	Not due
Initial	7	13	2	7	0	0
Discharge	21	5	0	3	0	0
1 Month	17	1	0	4	7	0
6 Month	19	1	0	2	1	6
12 Month	8	0	0	4	2	15
24 Month	5	0	0	0	2	22

9. HOW SUPPLIED:

The implant and delivery system are packaged separately. The delivery system is size matched to the implant. Both components are provided sterile. Product is sterilized via ETO.

10. DIRECTIONS FOR USE:

A. Detailed Product Description:

The CardioSEAL Septal Occlusion System consists of two primary components. The CardioSEAL (Occluder) is comprised of a metal alloy (MP35n) framework to which polyester fabric material has been attached.

From the center of the CardioSEAL, a small wire with a pin at its end extrudes out at approximately 90 degrees to the plane of the CardioSEAL. The CardioSEAL is attached to sutures through a loading funnel. The loader should always be connected via sutures to the side of the CardioSEAL opposite the side from which the pin wire extrudes.

The delivery catheter is comprised of a coaxial catheter shaft through which a spring guide travels, connected to a solid control rod. At the proximal end of the control rod, a control handle is connected to an inner control wire, which courses through the spring guide to the distal end of the catheter shaft, where it terminates within a small tubular sleeve. The control wire terminates at the distal end in a pin, for attachment to its mate on the CardioSEAL. When retracted, the pin slides inside the sleeve. The distal end of the catheter terminates in a pod. Retraction on the control rod moves the sleeve into the pod. Refer to figure 1 for an illustration of the delivery system and CardioSEAL.

B. CardioSEAL Size Selection and Inspection:

Selection of an appropriately sized CardioSEAL(O) should be based upon measuring the defect diameter through the use of a sizing balloon (stretched defect diameter – SDD), procedural angiography and/or transesophageal echocardiography, unless the size of the defect is known from the medical record. It is recommended that the CardioSEAL to Stretched Defect Diameter ratio (O:SDD) be 1.7-2.0:1 , and that the area containing the target defect be large enough to allow the CardioSEAL to fully deploy. The defect and surrounding structures should be fully examined in multiple planes to assure proper sizing of the CardioSEAL.

The Right Femoral Vein is recommended for vascular access although physicians should consider defect location and the route of introducer sheath travel relative to the potential for access in selecting the venous access site.

An 11F, 75cm long, hemostasis control introducer sheath with NIH type curve is recommended for CardioSEAL delivery. Sheath curve shape may need modification

based on individual patient conditions and defect location. As the use of long sheaths represents a potential risk of air embolus, care should be taken to insure adequate irrigation and 'backfilling' of the sheath with saline during removal of the dilator in order to avoid air entry.

A 14F or 16F short introducer sheath may be placed coaxially over the long introducer sheath prior to long sheath insertion if the physician believes the circumstances of the case raise the potential for device retrieval after attempted placement.

Prior to use, inspect the delivery system and CardioSEAL for signs of damage, such as kinks or bends in delivery wire or framework of the CardioSEAL. Check for secure attachment of the fabric to the framework.

Manipulate the delivery system and actuate the control handle to ensure that the attach release pin exits and retracts into the sleeve, and that the spring guide wire exits and retracts into the pod.

The delivery catheter system and CardioSEAL are packaged separately. Each is a component of the system, however, and each implant requires an equivalently sized or larger delivery catheter for appropriate use.

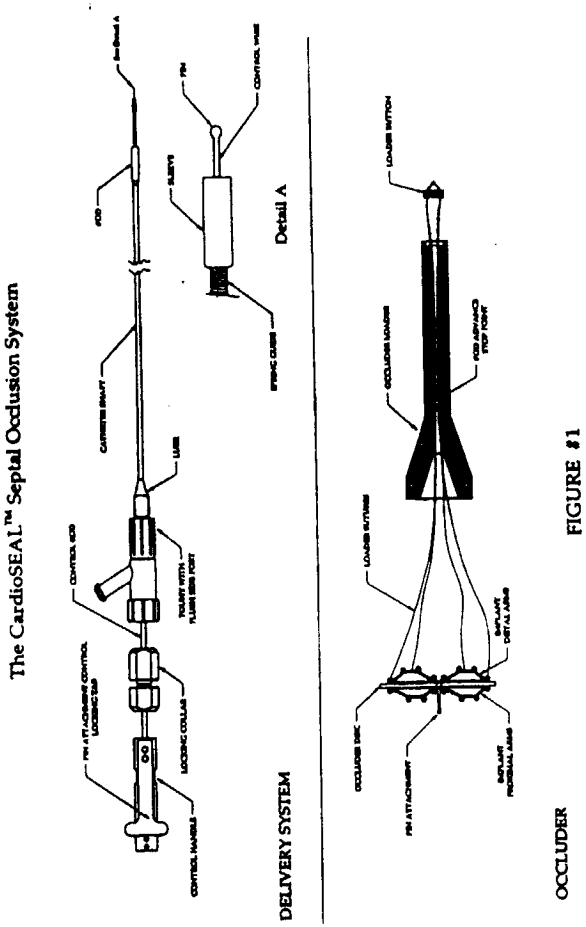


FIGURE #1

C. ***Preparation for Delivery:***

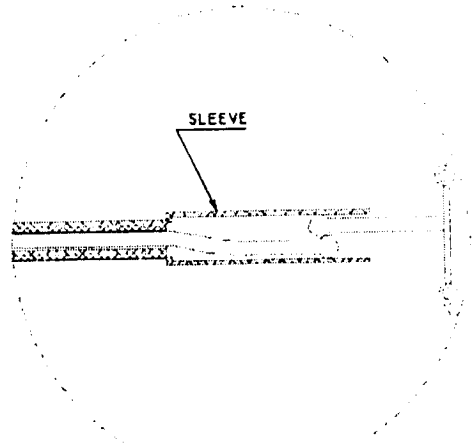
Attaching the CardioSEAL to the Delivery Catheter:

NOTE: Attachment and loading of the CardioSEAL *into the delivery catheter should not occur until*

a. *the defect has been determined to be of appropriate size and position to accomodate the CardioSEAL, and*
b. *access to the defect with an appropriate French size and length introducer sheath has been obtained.*

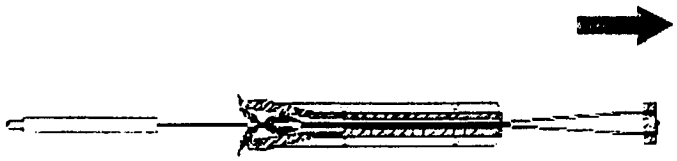
1. Loosen the black locking collar on the delivery catheter and advance the control rod until the sleeve exits from the pod. Pull gently upward on the pin control locking tab on the control handle. Push the rear section of the control handle in, extruding the pin from the sleeve about 3 – 4 mm.

2. Place the pin of the CardioSEAL into the sleeve, behind the pin extruding from the sleeve. Draw both pins into the sleeve by lifting up on the control handle tab and pulling the rear section of the control handle out. Seat control tab into slot on control handle, and test for secure attachment of CardioSEAL to delivery system with a gentle to and fro motion of the CardioSEAL.

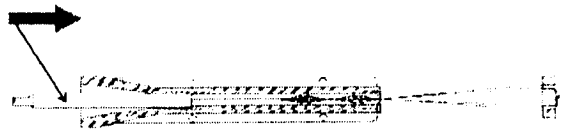


3. Submerge the loader/ CardioSEAL assembly in sterile saline and thoroughly soak the CardioSEAL. Make sure inner lumens of loader are wet. This will decrease friction between CardioSEAL and loader during loading.

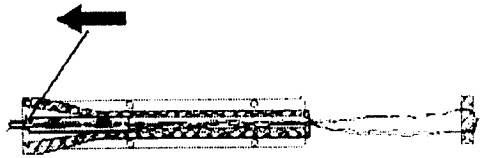
4. Carefully draw the CardioSEAL into the smallest section of the loader by pulling on the loader button. Do not attempt to force CardioSEAL into funnel section of the loader unless all four arms on each side of the CardioSEAL are appropriately retracted into the collapsed position.

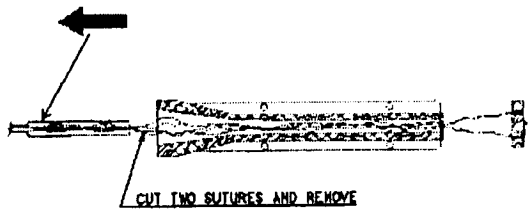


5. With the CardioSEAL fully collapsed in the smallest section of the loader, use the control rod to advance the pod into the loader until the pod contacts the stop point.



6. Holding the pod firmly in the loader, retract CardioSEAL into the pod through the use of the control rod. Once in the pod, remove pod from loader, snip sutures one at a time, and remove from the CardioSEAL. Discard loader, sutures and loader button.



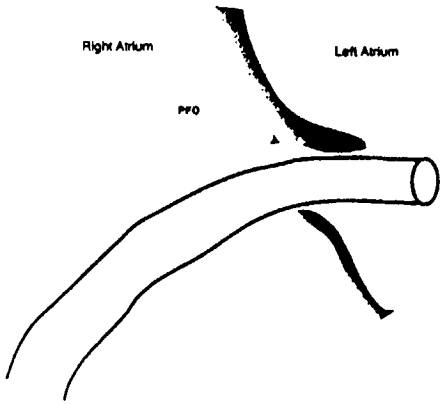


7. Loosen locking collar and advance it up to the Y-body. Tighten locking collar and flush the delivery system with normal saline several times to remove all air from the system. The CardioSEAL is now ready for delivery to the defect.

D. Insertion

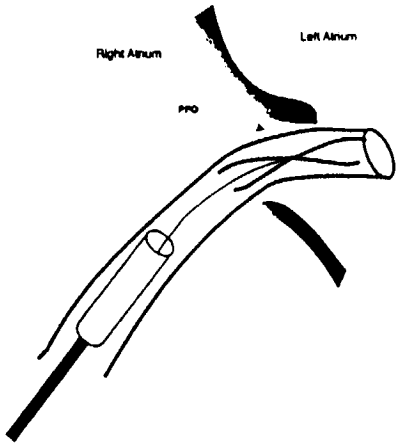
NOTE: As previously discussed in Section C, Preparation, Note B, an introducer sheath of sufficient French size (11F) for the CardioSEAL *and of adequate length to reach the target defect should have been placed via the venous system across the defect.*

1. Reposition sheath across the defect so that the distal tip of the sheath is approximately 1cm into the distal side of the defect. Thoroughly irrigate the previously placed introducer sheath to minimize risk of air entry and air embolus.

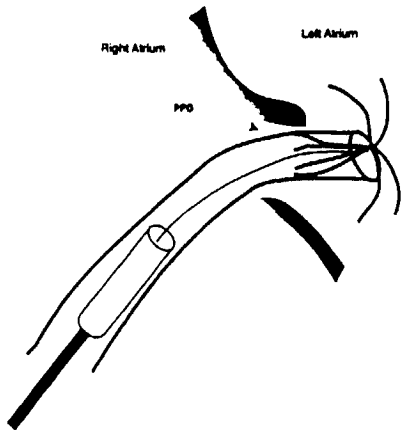


2. Insert the pod of the delivery system into the sheath, and advance until the pod is no closer than 5 to 10 cm from the tip of the sheath. The pod should be in the fluoroscopic field of view.

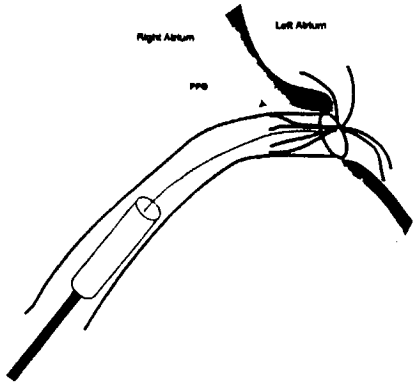
3. Loosen the locking collar nut and advance the collapsed CardioSEAL out of the pod and into the sheath. The CardioSEAL will remain collapsed within the sheath, with the sheath serving as an extension of the pod. Continue to advance the CardioSEAL until it is within 1-2mm of the tip of the sheath.



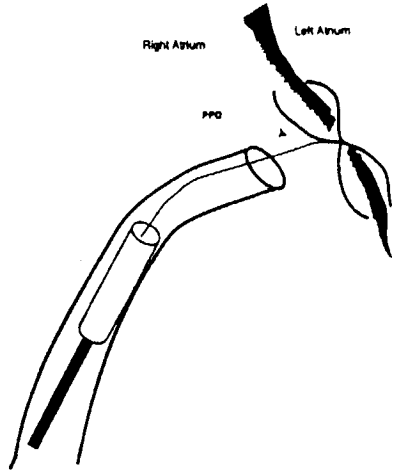
4. Recheck sheath tip position to verify location on distal side of defect. Holding the sheath and catheter steady, advance the distal set of CardioSEAL arms out of the sheath by moving the control rod forward. Alternatively, open distal set of CardioSEAL arms by retracting sheath off of the distal arms. Under fluoroscopy and Transesophageal echo, ascertain that all four distal CardioSEAL arms have fully deployed and are intact.



5. Holding the sheath and catheter steady, retract entire sheath – catheter - CardioSEAL system until the distal CardioSEAL arms approximate or engage the distal wall of the defect.

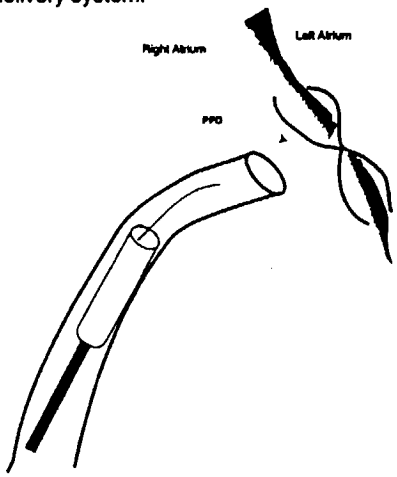


6. Once approximated or engaged, retract CardioSEAL further to slightly flex the CardioSEAL arms. Retract sheath off of proximal CardioSEAL arms while maintaining position in the defect. This will release the proximal arms of the CardioSEAL to engage the proximal defect wall.



7. Allow delivery catheter and sheath to assume a neutral (i.e. no retraction) position and confirm correct placement of all arms on appropriate sides of the defect.

8. Once proper positioning is confirmed, advance the pin from the sleeve using the control handle at the proximal end of the delivery system. This will release the CardioSEAL from the delivery system.



9. Remove delivery system from sheath.

11. PATIENT INFORMATION:

The following counseling information should be provided to the patient:

Patients should be reminded of the importance of adhering to their aspirin and endocarditis prophylaxis regimens.

If an MRI is required, the patient should inform MRI staff of the presence of the CardioSEAL.

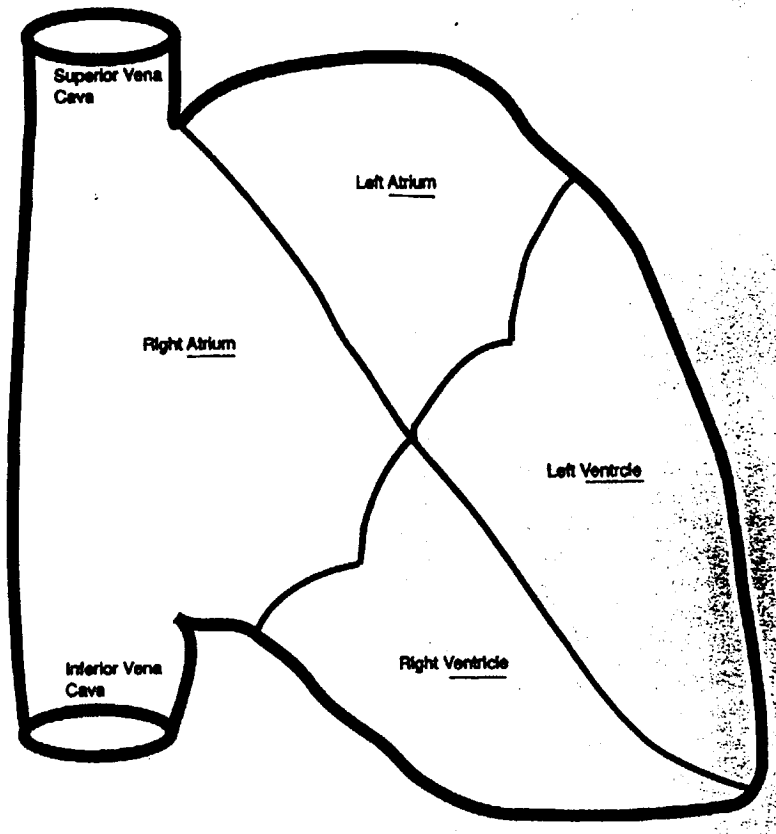
Patients should be encouraged to contact their physician if they have any questions or concerns

A patient brochure is available and is entitled: "A Patient's Guide to Transcatheter Defect Closure using the CardioSEAL® Septal Occlusion System."

PL#:0256.00

NMT
MEDICAL

A Patient's Guide to Transcatheter Hole Closure of a Patent Foramen Ovale using The CardioSEAL® Septal Occlusion System



Basic Diagram of the Normal Heart

Humanitarian Use Device

The CardioSEAL Septal Occlusion System is authorized by Federal (USA) law as a Humanitarian Use Device for use in the following indication only:

36

The CardioSEAL Septal Occlusion System is indicated for the closure of a patent foramen ovale (PFO) in patients with recurrent cryptogenic stroke due to presumed paradoxical embolism through a patent foramen ovale and who have failed conventional drug therapy.

Cryptogenic stroke is defined as a stroke occurring in the absence of potential known cardiac, pulmonary, vascular or neurological sources. Conventional drug therapy is defined as a therapeutic dosage of oral anticoagulants.

The effectiveness of this device in this indication has not been demonstrated.

Note: underlined words are defined in the Glossary of technical term.

Introduction:

You have been diagnosed by your physician as having a small hole in your heart called a Patent Foramen Ovale (PFO) which is suspected as being the pathway for a small embolus to have traveled from the right atrium to the left atrium (see diagram below). This embolus resulted in a blockage of blood flow to an artery, resulting in a paradoxical embolic event, such as a stroke. You may have had this event multiple times despite taking blood thinners.

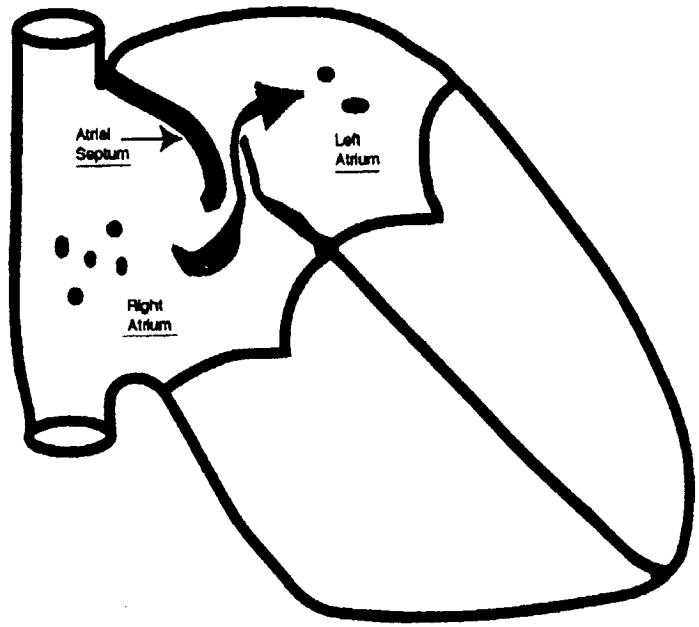
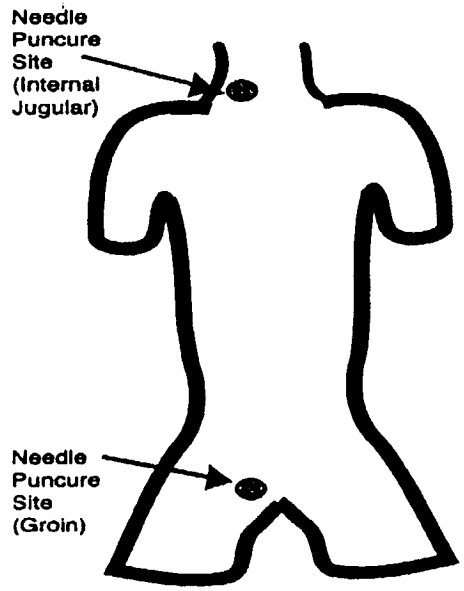


Diagram of a the Heart with a Patent Foramen Ovale (PFO)

Diagram illustrating blood flow through a Patent Foramen Ovale. The PFO is the opening through which the blood is able to flow when the pressure in the right atrium is greater then the left atrium.

Your physician has recommended that this small hole should now be closed using an implant. The implant is placed in the heart using a catheter. This procedure is called Transcatheter Hole Closure. It is an alternative to open heart surgery. The physician believes that the risks of open heart surgery to close this hole presents an unusually high risk to you. Transcatheter Hole Closure is a procedure that avoids the need for open heart surgery. As a less invasive procedure, it is believed to present fewer risks since open heart surgery is avoided.

How does Transcatheter closure work?
Transcatheter Hole Closure is performed in the Cardiac Catheterization Laboratory by a Doctor. The Doctor will gain access to your (your child's) heart by getting access to a major vein in the groin or internal jugular vein.



This is done by a needle puncture. Various catheters will be advanced from the groin or neck into the heart. A test involving moving pictures of the heart, called an angiogram, will be taken to better visualize the heart and the hole. The Doctor may use a special ultrasound device, called TransEsophageal Echocardiography (TEE). This is another way to better see the heart and the hole. The TEE involves putting a probe into the esophagus, the tube between the mouth and stomach. These tests are used to determine which size implant the physician will use to close the hole.

The appropriate size implant is attached and collapsed for placement into a special catheter. The catheter is then advanced to the site of the hole. The Doctor re-expands the implant so that part of it sits on each side of the hole. In effect the hole is gently sandwiched between the two sides of the implant. The implant is then released from the catheter. The catheter is removed and the procedure completed.

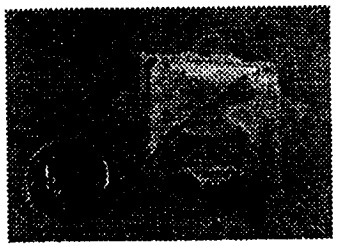
Diagrams showing the basic steps of the procedure.

38

Will I be awake during the procedure?
This is up to the physician. Many patients are put under general anesthesia for this procedure. A local anesthetic is used to numb the groin or neck (the location where the catheters are inserted).

How does the implant stay in place?
CardioSEAL is made from two, small diameter wire frameworks. The framework has a special fabric attached to it. The device looks like two little umbrellas set edge to edge. Each umbrella framework has special springs. This allows the umbrellas to spring towards the hole. This very slight tension, along with the blood in the heart, holds the device in place. Over time, tissue grows into the fabric and the implant becomes part of the heart.

What does the Implant look like?
CardioSEAL comes in several sizes. The smallest (17mm measured diagonally) is about the size of a dime, the largest is about size of a half- dollar. This picture shows one of the larger implants placed next to a dime. This may give you some perspective of the size. The framework is made from a metal frequently implanted in the body during other surgeries. The fabric is the same fabric the surgeon would use if open heart surgery was performed.



What are the risks?
The risks are similar to those associated with other heart catheterization procedures. There are additional risks associated with the implant. Examples include:

- dislodgement
- incomplete sealing of the hole
- abnormal heart rhythms
- bruising at the groin or arm
- changes in blood pressure
- air embolus
- hemolysis
- apnea
- headache/migraine
- infection including endocarditis
- perforation of vessel or myocardium
- thromboembolus
- stroke or TIA
- valvular regurgitation
- fracture of the implanted device
- palpitations

The implanting physician usually insures that the risks associated with heart catheterization and the implant are reviewed with each patient.

Will the procedure hurt?
Usually not. After the procedure, some patients report tenderness at the groin or arm. Some also complain of a sore throat from the TEE probe. Patients cannot "feel" the implant.

What is the special care after the procedure?

- bed rest for a period of time (this allows the implant to firmly stabilize)
- restriction from heavy lifting or other physical activities for a period of time
- take a blood thinning product, such as Aspirin, every day, for a period of time (perhaps six months or longer)
- take antibiotics to prevent infection for a period of time (perhaps six months or longer and when going to the dentist or having a minor surgical)
- follow the doctor's instructions precisely
- call the doctor if there are any questions

What about follow up visits?

All patients are asked to see their doctor for follow up visits. The Doctor will provide specific instructions for follow-up care.

Does the Implant stay in for the rest of my life?

Yes, it is intended to stay in forever.

Can I go through metal detectors, or have an M.R.I?

Yes. The implant will not set off metal detectors. The metal framework is not magnetic. It will not be affected by an MRI, but the picture taken by the MRI might have a fuzzy quality. If an MRI is needed, the MRI staff should be informed about the presence of the implant.

What are the options or alternatives to this treatment?

Having open heart surgery to close the PFO is an option. Continuing to take blood thinners is also an option. Or, you may elect to have no treatment of any kind.

What are the contraindications to this treatment?

- presence of blood clots in the vein used to introduce the catheter
- the vein needed to introduce the catheter is too small for the catheter to fit
- presence of an active infection
- patient unable to take aspirin or other blood thinning medication

Glossary of technical terms

- **Abnormal heart rhythms** – abnormal heart beats.
- **Air embolus** – an air bubble in the blood stream.
- **Angiogram** – a test involving moving pictures of the heart.
- **Apnea** – a transient cessation of breathing.
- **Atrium** – the upper two chambers (right and left) of the normal heart.
- **Cardiac Catheterization Laboratory** – a room in the hospital dedicated to accessing the heart using catheters and X-ray guidance.
- **Catheter** – a sterile tube for insertion into a vessel to permit injection or withdrawal of fluids or to pass material through.
- **Cryptogenic** – an unknown source.
- **Dislodgement** – moving from its intended position.
- **Endocarditis** – an inflammation of the lining of the heart and its valves.
- **Embolus** – an abnormal particle circulating in the blood.
- **Esophagus** – the tube between the mouth to the stomach.

- **Heart catheterization** – a less invasive way (compared to open heart surgery) to access the heart using the arteries of veins.
- **Hemolysis** – breaking of the red blood cells.
- **Implant** – a medical device which is put into the body.
- **MRI** – Magnetic Resonance Imaging--a type of test used to visualize body tissue that uses a magnetic field.
- **Palpitations** – an abnormally rapid heart beat.
- **Paradoxical Embolic Event** – a medical event in which a small clot or piece of debris from the venous system crosses over to the atrial system creating a condition where blood flow in the artery is blocked.
- **Patent Foramen Ovale (PFO)** – a term used to describe a small hole in the section of the atrial septum that is called the Foramen Ovale.
- **Perforation of vessel or myocardium** – a tear in a blood vessel or the heart.
- **Probe** – a flexible, tube-like medical instrument designed to enter different body cavities.
- **Pulmonary Arteries** – major blood vessels that direct blood from the heart to the lungs.
- **Stroke** – an abrupt onset of neurological symptoms caused by decreased blood flow or bleeding in the brain.
- **TransEsophageal (TEE)** – an ulstrasound (sound waves) test to visualize the heart and hole.
- **Thromboembolus** – a blood clot within a blood vessel.
- **TIA** – (transient ischemic attack) a transient lack of oxygen to the brain.
- **Transcatheter Hole Closure**- a less invasive procedure (compared to open heart surgery) used to close heart holes using catheters.

- **Valsalva maneuver** – term used to describe a condition created by the patient when they block exhalation and increase pressure in the chest cavity by contracting the muscles of the stomach and chest. Typically, many people perform a valsalva maneuver when they have a bowel movement.
- **Valvular regurgitation** – an abnormal backward flow of blood through a valve.
- **Ventricle** – the lower two chambers (right and left) of the normal heart.

This guide was prepared by Nitinol Medical Technologies, Inc. It is based on input and guidance from Physicians and Clinical Staff throughout the United States. NMT wishes to thank them for their contributions. However, this guide is not a replacement for speaking with your physician. We recommend you write down questions for your doctor on a separate piece of paper.

 ML#0024.00